Health Officials Seek Ways to Halt AIDS

A recent workshop considered the options for preventing the spread of the new immune disease; an easy solution is unlikely

On 4 January the Centers for Disease Control (CDC) convened a workshop at its Atlanta headquarters to assess the options for halting the spread of the new disease called acquired immunodeficiency syndrome or, more commonly, AIDS. The main topic of discussion was the possibility that the disease, which may kill up to 70 percent of the patients within 2 years of diagnosis, might be spread in blood and blood products.

The CDC recently reported that hemophiliacs are at high risk of contracting AIDS, which may be transmitted by an infectious agent in the blood clotting factor preparations that they take (*Science*, 7 January, p. 42). The Center's Bruce Evatt told the workshop that AIDS was the second leading cause of death for hemophiliacs in 1982, even though the disease was first discovered in hemophiliacs in the summer of that year. Eight hemophiliacs who had none of the other known risk factors died from AIDS, compared to some 40 who died of bleeding. James Curran, head of the CDC task force investigating AIDS, says, "The sense of urgency is greatest for hemophiliacs. The risk for others [who receive blood products] now appears small, but is unknown."

Suspicion has been cast on blood products in addition to clotting factor, however. An infant contracted AIDS after receiving red blood cells that had come from a man who developed the disease several months after he donated the blood. The CDC is also investigating the cases of two adults who developed AIDS after receiving blood transfusions during surgery. The two did not belong to any of the known high-risk groups, which include, in addition to hemophiliacs, homosexual and bisexual men who are extremely active sexually, users of intravenous drugs, and Haitians. In each case, investigators have identified a blood donor who has certain characteristics associated with AIDS, including a particular immune defect, although neither donor has actually developed the disease.

The CDC investigators have also identified several AIDS patients who donated blood. None of the recipients has contracted the condition, but there is still cause for worry. Thomas Spira of the CDC points out that there may be a long lag period, a year or more, between the time of exposure to the causative agent and the onset of AIDS. In other words, although there is currently no firm evidence linking ordinary blood transfusions to transmission of the disease, it is too early to rule out such a link.

The workshop participants easily reached agreement on some preventive measures that might check the spread of AIDS. About 75 percent of the AIDS victims are homosexual or bisexual men in whom the disease is thought to be sexually transmitted. There was general agreement that homosexual men should avoid sexual contact with known or suspected AIDS patients, minimize the number of their sexual partners, and refrain from anonymous sexual contacts. Heterosexuals might follow the same suggestions because, according to Curran, there are indications that AIDS may also be transmitted by heterosexual sex and other forms of intimate personal contact, such as that between mother and child.

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The seriousness of the threat of AIDS transmission by blood products and what, if anything, ought to be done in the current state of uncertainty remained thorny issues for the workshop participants. Not everyone agrees with the conclusion, accepted by CDC officials and many other investigators, that AIDS is caused by an infectious agent, presumably a virus, which could contaminate blood products. Louis Aledort, the medical director of the National Hemophilia Foundation, says, "I think it is too easily concluded that there is a transmissible agent. I can't rule it out but the data are not there yet." Aledort favors the idea that hemophiliacs, as well as homosexuals and intravenous drug users, because they are exposed to a great number of foreign antigens, experience a high degree of antigenic stimulation that effectively wears out their immune systems.

Nevertheless, because of the seriousness of AIDS, many participants were in favor of introducing measures to prevent persons who might be carrying an infectious agent from donating blood or plasma. The question is how to do this, especially in view of the long latent period of the disease and the possibility that many individuals who do not have full-blown AIDS may have a milder form or be asymptomatic carriers of an infectious agent.

Asking members of high-risk groups to voluntarily refrain from donating blood is one relatively uncontroversial approach, although it would probably not eliminate all potential carriers. Automatically excluding all members of high-risk groups is another, although this measure has the disadvantage of stigmatizing all homosexual males when only a fraction—those who are extremely sexually promiscuous—are likely to transmit an AIDS agent. Past and present users of intravenous drugs, who may be hepatitis carriers, and hemophiliacs are already excluded. Potential donors may also be screened for AIDS symptoms through a physical examination or a medical history.

Finally, the blood itself may be screened. Since the agent has not been identified, it would be necessary to use a "surrogate agent" as a marker for AIDS infectivity. The best candidate for this is an antibody to the core antigen of the hepatitis B virus. According to Spira, testing for this antibody in donated blood would detect about 90 percent of the donors who might transmit an AIDS agent, including persons with full-blown AIDS, those with the milder symptoms, and members of high-risk groups.

Some workshop participants favored requiring the test for all blood collection centers, but Aaron Kellner of the New York Blood Center dissented. "It is one thing to do these tests in the laboratory and another in the real world," he said. Kellner suggests that a few blood collection centers in the cities where AIDS is most prevalent—New York, San Francisco, and Los Angeles—undertake pilot

studies to assess the feasibility and costs (including lost blood donations) of doing the antibody test.

The next step after the workshop is the preparation by CDC officials of a list of options for containing AIDS. This list will be submitted to Edward Brandt, assistant secretary for health in the U.S. Department of Health and Human Services, whose office will decide which options, if any, to implement.

Meanwhile, hemophiliacs who need clotting factor face an uneasy situation. Oscar Ratnoff, a hemophilia specialist from University Hospitals in Cleveland, proposes that they might minimize their risk of AIDS by using clotting factor cryoprecipitate instead of concentrate. A given lot of cryoprecipitate is made from material donated by one individual whereas each lot of concentrate contains material from an average of 5000 donors.

Cryoprecipitate may not be potent enough to control bleeding of some patients, however. The National Hemophilia Foundation recommends that new patients be given cryoprecipitate as long as possible, but that hemophiliacs who are already using the concentrate continue to do so. According to Dennis Donohue of the Bureau of Biologics of the Food and Drug Administration, an effort to prepare a safer clotting factor concentrate by removing or inactivating contaminating viruses is under way.

The biggest question of all still remains. What causes AIDS? Donald Armstrong of Memorial Sloan-Kettering Cancer Center expressed the hope that investigators not be distracted from answering that question. "I have no doubt that this is an infectious disease," he asserted. "I think we have to find the agent. A surrogate agent isn't good enough."—**JEAN L. MARX**

Orbital Variation—Ice Age Link Strengthened

The geological evidence is stronger than ever, and realistic mechanisms for the connection are being proposed

Palisades, New York. Climate cycles related to astronomical influences seemed to be popping up everywhere at last month's meeting* here on Milankovitch and climate. Climatic responses to variations in Earth's orbit and axis of rotation appeared in geological records of the upwelling of seawater off Arabia, the blowing of dust across the Pacific, and the flow of deep currents in the Atlantic. Researchers presented evidence that processes as diverse as the monsoon of 9000 years ago and the chemistry of a briny lagoon of 250 million years ago pulsed to the same orbital beat.

The gathering was not simply a celebration of Milutin Milankovitch's suddenly popular theory of climatic change. Researchers presented new evidence that seems finally to have laid to rest the argument that orbital variations might cause minor climate fluctuations but not major climatic changes such as the ice ages, the largest and most abrupt climatic changes known. Researchers are also beginning to postulate reasonable mechanisms to explain the amplification of the orbital signals and their reverberation throughout the climate system.

A major problem with convincing skeptics of a possible link between orbital cycles and the ice ages had been an embarrassing failure of Milankovitch's theory. The most obvious climate cycle in the geological record is the recurrence of ice ages about every 100,000 years. But the 100,000-year orbital cycle of changing eccentricity alters the total sunlight falling on Earth each year, called insolation, by 0.1 percent at most. That is hardly the makings of an ice age, critics noted. Perhaps the synchroneity of the two cycles over the past few hundred thousand years was only a coincidence?

Members of the spectral mapping group (SPECMAP), a collaboration of researchers from five universities, have used some of the orbital cycles themselves to sharpen up the geological record and demonstrate that the eccentricity and glacial cycles have been in step for at least the past 800,000 years, an unlikely coincidence. They measured the oxygen isotope composition, which reflects the amount of glacial ice in the world, down three deep-sea sediment cores. They knew that the slowly accumulated microfossils beneath the sea floor did not perfectly preserve the glacial climate record, but they knew also that shorter period orbital variations had been recorded in the same distorted isotopic records. Earth's axis of rotation had been gently nodding back and forth about its tilted position every 41,000 years or so, and the direction its axis pointed toward the stars had drifted, or precessed, in a circuit every 23,000 years. The known effects on climate of these predictable orbital variations, together with four radiometrically dated points in each core, thus provided an internal clock to which the isotope records of the three cores could be adjusted.

Once SPECMAP workers had adjusted the climatic records of the three sediment cores to make the best match with the known short-period orbital variations, they found that the amplitude of each of the main eccentricity cycles of the past 800,000 years was proportional to the amplitude of the corresponding 100,000-year glacial cycle, according to John Imbrie of Brown University and SPECMAP. The correlation between the two near the 100,000-year frequency explains about 77 percent of the climate variance. On the basis of standard statistical techniques, Imbrie concluded that orbital variations accounted for 60 ± 10 percent of climatic variability in the range from 19,000 to about 100,000 years per cycle. Orbital variations are thus "the fundamental cause of the succession of the Pleistocene ice ages of the past 800,000 years," he declared.

Although some had questioned such uncompromising statements about the control of the ice ages (*Science*, 14 July 1978, p. 144), no one rose on this occasion to object. Not everyone would stand by that specific number; most felt that the statisticians could be left to fight over the meaning of such a calculation. Instead, the geologists and paleoclimatologists, now thoroughly convinced of the connection, are eager to use orbital variations to sort out how climate varied in the past and what processes intervene between orbital variations and climate.

One of the great mysteries has been how such large climatic changes could be prompted by such small effects on insolation. Only eccentricity variations

*Milankovitch and Climate: Understanding the Response to Orbital Forcing, held 30 November to 4 December 1982 at Lamont-Doherty Geological Observatory, Palisades, New York. The cochairmen were André Berger and John Imbrie.